

WE CLAIM:



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A method comprising.

- a) altering a chromosomal sequence of a donor nucleus of a donor cell by introducing a pair of single-stranded targeting polynucleotides, and a recombinase into said donor nucleus of said donor cell, wherein said pair of targeting polynucleotides are substantially complementary to each other and each comprising a homology clamp that substantially corresponds to or is substantially complementary to a predetermined DNA sequence of said nucleus; and.
- b) transplanting said nucleus into an oocyte to produce a recombinant zygote.
- 2. The method of claim 1 further comprising:
 - c) activating said recombinant zygoté.
- The method of claim 1 or 2 further comprising: 3. 15
 - d) transfering said recombinant zygote into a surrogate mother.
 - 4. The method of claim 3 further comprising:
 - e) harvesting a transgenic offspring of said mother.

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- The method of claim_4 further comprising: 5.
 - breeding said offspring.
- 6. The method of claim 1 wherein said recombinase is RecA.

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The method of claim 6 wherein said RecA is E. coli RecA. 7.

The method of claim it wherein said recombinase is Rad51.

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- The method of claim wherein said donor nucleus is an isolated nucleus.
- The method of claim 1 wherein said donor cell is selected from the group consisting of a 10 haploid cell, a diploid cell, a somatic cell, an embryonal cell, and a fetal cell.
- The method of claim 10 wherein said haploid cell is selected from the group consisting of a 11. 35 germ cell, a germ cell precursor, a germ stem cell, and a gametocyte.
 - The method of claim 10 wherein said somatic cell is selected from the group consisting of a 12. mammary derived cell, an adult tail-tip cell, a cumulus cell, an epithelial cell, a dermal cell, a

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keratinocyte, a mesenchymal cell, a stem cell, a blood cell, and a fibroblast.

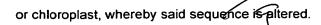
- 13. The method of claim 10 wherein said embryonal cell is selected from the group consisting of an embryonal germ cell, an embryonal stem cell, an umbilical cord cell, an umbilical cord blood cell, an endodermal cell, a mesodermal cell, and an endodermal cell.
- 14. The method of claim 1 wherein said oocyte is an enucleated oocyte.
- 15. The method of claim 1 wherein said oo cyte is arrested in metaphase of meiosis II.
- The method of claim 1 wherein said occyte is selected from the group consisting of a rodent, ungulate, bovine, ovine, canine, feline, simian, rabbit, equine, fish, amphibian, reptile, crustacean, and mollusc oocyte.
- 15 17. The method of claim 1 wherein said transplanting is by microinjection, electrofusion, or piezo driven micropipet injection.
 - 18. The method of claim 2 wherein said activating occurs about 6 hours or less after said transferring step.
 - 19. The method of claim 2 wherein said activating is by electroactivation.
 - 20. The method of claim 2 wherein said activating is by contacting said recombinant zygote with a chemical activator.
 - The method of claim 20 where a said activator is selected from the group consisting of Ca²⁺ release stimulators, Ca²⁺ ionophores, strontium ions, sperm cytoplasmic factors, inhibitors of protein synthesis, oocyte receptor ligand mimetics, regulators of phosphoprotein signaling, and ethyl alcohol.
 - 22. A method comprising introducing a spermatozoa, a pair of single-stranded targeting polynucleotides, and a recombinase into an oocyte, wherein said pair of targeting polynucleotides are substantially complementary to each other and each comprising a homology clamp that substantially corresponds to or is substantially complementary to a predetermined DNA sequence of said spermatozoa and/or said oocyte whereby a recombinant zygote is produced.
 - 23. The method of claim 22 further comprising:
 - b) activating/said recombinant zygote.

The method of claim 23 further comprising:

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recombinase, wherein said pair of targeting polynucleotides are substantially complementary to each other, and each comprising a homology clamp that substantially corresponds to or is substantially complementary to a predetermined nucleic acid sequence of said mitochondria



- 39. The method of claim a wherein said cell is a plant cell.
- The method of claim 38 wherein said pair of single-stranded targeting polynucleotides, and a recombinase are introduced into said cell by biolistics.